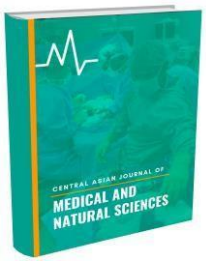

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Article

Evaluation of Biomarker and Clinical Indicators in Women with Breast Cancer in Kirkuk Governorate: A Comparative Study

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Abstract: Being one of the commonest cancers among women (and rank as leading cause of death in women) makes breast cancer a global problem and Iraqi experience is not different. This study was conducted to assess some biochemical, clinical and prognostic indicators among women diagnosed with breast cancer in Kirkuk Governorate (Iraq) as compared to a control group of apparently healthy women. The clinical parameters included tumor diameter, hormone receptor status (ER/PR), HER2 expression and lymph node metastasis and biochemical indicators such as CA 15-3, CEA, CRP and LDH. Results demonstrate the differences of these biomarkers between these two groups, showing potential for effective diagnosis and prognosis of breast cancer. The study included 90 women: 60 with breast cancer and 30 without it. The data showed that the proportion of patients with larger-size tumor, HER2-positive patient and more positive nodes in the patient group were significantly higher. Additionally, key biomarkers CA 15-3, CEA, CRP and LDH were also increased in breast cancer group suggesting potential for use of these markers for both diagnosis and follow-up of the disease. Tumor characteristics, hormone receptor status, and the prevalence of lymph nodes among breast cancer patients showed significant differences in our study being compared to controls. The levels of CA 15-3, CEA, CRP and LDH are increased in the patient group indicating that these biomarkers may be useful for confirming the presence of breast cancer and monitoring its behavior**.** This study emphasizes the clinical and biochemical markers have their importance in diagnosis, prognosis as well as monitoring for breast cancer burden to different districts like Kirkuk Governorate. Studies in this area should continue to improve treatments and prevent poor outcomes for patients.

Keywords: : Breast Cancer, Biomarkers, CA 15-3, CEA, HER2, Prognosis, Tumor Size, Ki67, Kirkuk

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1. Introduction

Next to lung cancer, breast cancer is the second most frequent non-skin type of cancer and ranks fifth as cause of death due to cancer in women, contributing 10.4% of all incidences [1]. Breast cancer and Iraqi women According to the latest statistics of 2019 nearly one-third of all reported cases in Iraq was a breast cancer depicting largely as number one killer among diseases diagnosed in all ages[2]. Breast cancer is the most common type of cancer in women in Iraq, accounting for one in three cancers among women nationwide, according to the latest Iraqi Cancer Registry. This illustrates that for the population at large in Iran, breast cancer appears to exceed bronchogenic carcinoma in frequency. Early detection and screening, when combined with appropriate treatment, probably offer the greatest possibility for an immediate reduction in breast cancer mortality as the World Health Organization (WHO) reports. In 2001, the Iraqi national program for early detection of breast cancer was launched aiming to detect and diagnose

the disease in its early stages. Since then, all the main hospitals in Iraq provinces have established clinics and centers for early detection of breast cancer. Mean age of diagnosis in research conducted on patients from the three northern Iraqi governorates (47.4 ± 11.0 years) was also shown in this study to be comparative/not higher than any other research in the same field, as reviewed recently by Newman:500 who reported that it ranged from 40 to 50 years [16-22]. Breast cancer is diagnosed at late clinical stages in most cases, the majority of which are those aged ≤ 50 years patients living in Sulaymanyia- Iraq. Data from reports on patients diagnosed with breast cancer in the central region of Iraq supplied more characterizing information of the incidence and clinic-pathological aspects review for these regions (Baghdad, Ramadi-Falluja, Mosul, Middle Euphrates area). Breast cancer in most cases hits females, Basrah reports. According to the authors, breast cancer is more common in industrialized countries than developing nations, due both to lifestyle and risk factors and improved detection techniques. According to some studies, the proportion of breast cancer cases is increasing markedly in various parts of Basrah, Iraq[3]. Breast cancer (BCa) is one of the most common cancers among women in the world and represents the highest mortality rate among Iraqi woman [4].

The five main risk factors for developing breast cancer include: your age, family medical history, estrogen exposure, reproductive factors and lifestyle. Old age is the biggest risk to these due to their associated with the illness and increasing of commonness of the disease. By family history, almost 25% cases of breast cancer are affected. It is three times more likely in women who have a family member, such as a mother or sibling, with the disease. Reproductive variables like early menarche, delayed menopause, age at first pregnancy as well as low parity also put several women at increased risk for breast cancer. A link is suspected between endogenous (produced within the body) and exogenous (from outside the body) estrogens and an increased risk of breast cancer. Ovariectomies can reduce breast cancer risk in premenopausal women cuz ovary [5]. It is progesterone that is required to control the normal mammalian female reproductive physiology [6] for one of these sex steroid hormones are estrogen, and all exogenous synthetic progestogens (progestins) when used in combination with estrogen as menopausal hormone therapy or as a type of contraception increase the risk of breast cancer [7,8]. Breast cancer is one of the most common cancers among women worldwide, posing a significant health challenge due to the high incidence and mortality rates associated with it [9]. Early diagnosis and effective treatment require a precise understanding of the biological and clinical indicators that can assist in evaluating the disease and determining its course [10]. Biomarkers play a crucial role in cancer diagnosis, predicting its severity, and monitoring treatment response [11].

Biomarkers of breast cancer include proteins in the blood or tissue and genes [12]. The most common tumor markers for BC monitoring are cancer antigen 15-3 (CA 15-3) and carcinoembryonic antigen (CEA), among these. [13] Furthermore, C-reactive protein (CRP) and lactate dehydrogenase (LDH), as inflammatory markers are involved in cancer development and its course [14]. The global burden of breast cancer remained high where an estimated 2.3 million new cases and 670,000 deaths occurred in the year of 2022 [15]. The numbers of death percentage and incidence rate related to CRC are forecasted to increase greatly in the next decade, accenting that a better prevention, diagnosis and treatment ramp up approach must be performed [16]. The essential value of biomarkers in breast cancer management reveals itself from the onset with their critical role in early diagnosis, treatment monitoring and targeted therapy guidance [17].

2. Materials and Methods

Study Design and Setting

The purpose of the present cross-sectional analytical study conducted in Kirkuk Governorate, Iraq, in collaboration with oncology units and diagnostic laboratories

affiliated to hospitals and specialized medical centers for breast cancer diagnosis and treatment from April 20th, 2025 -to- July 28th, 2025.

Study Sample

The study included 90 women, divided into two groups:

a. **Patient Group:** 60 women diagnosed clinically and pathologically with breast cancer.
b. **Control Group:** 30 healthy women, matched by age and gender, with no history of breast cancer or chronic diseases affecting the markers under study.

Inclusion Criteria

a. Patients with histopathologically confirmed breast cancer in women.
b. Between the ages of 25–55.
c. No any chemotherapy or radiotherapy before the sample was obtained.

Exclusion Criteria

a. Chronic diseases e.g., liver or kidney disease.
b. Secondary breast cancer (other tumors and/or metastases).

Clinical and Diagnostic Data

The following clinical data were obtained from medical records and imaging tests: Age at diagnosis Tumor size Hormone receptor status (ER/PR) HER2 expression level Number of positive lymph nodes Clinical stage Tumor grade Ki-67 proliferation index

Sample Collection

Venous blood of 5 mL was collected from all patients in the morning following a 8-h overnight fasting period. Serum was separated through centrifugation at 3000 rpm for ten minutes to dry tubes, and stored in microtubes at -20°C until being analyzed.

Biochemical Assays

The following biochemical measurements were used: CA 15-3 (U/mL) — carried out through the enzyme-linked immunosorbent assay (ELISA) technique, using commercial kits from Roche Diagnostics (Switzerland); CEA (ng/mL) performed by ELISA technique and with certified kits from BioRad; CRP (mg/L)— since our center has its own laboratory service available, we used the immunoturbidimetric method performed by the analyzer Cobas 6000 of Roche Diagnostics. LDH (U/L): measured by the colorimetric assay method with a Hitachi 902 analyzer, using commercial reagents from using Hitachi High-Tech (Japan).

Statistical Analysis

Data were entered into SPSS (version 19), and results were expressed as mean ± standard deviation (Mean ± SD). Independent samples T-test was used for comparing the two groups. A p-value ≤ 0.05 was considered statistically significant.

3. Results

The following tables present the statistical results of the clinical, prognostic, and biochemical markers evaluated in this study, comparing the breast cancer patient group with the control group.

Clinical Indicators

Table 1. Clinical Indicators Result.

Clinical Indicator	Patient Group (Mean ± SD)	Control Group (Mean ± SD)	P-value
Age at Diagnosis	**49.20 ± 6.80**	**47.50 ± 7.10**	**0.224**
Tumor Size (cm)	**3.10 ± 1.20**	**1.10 ± 0.60**	**0.0001**

Hormone Receptors (ER/PR) (%)	**68.00 ± 10.00**	**72.00 ± 8.50**	**0.043**
HER2 Expression (%)	**23.40 ± 6.20**	**12.10 ± 5.80**	**0.0**
Positive Lymph Nodes	**2.70 ± 1.40**	**0.30 ± 0.50**	**0.0**

The results shown in the above table indicate statistically significant differences in most clinical markers between the breast cancer patient group and the control group. Tumor size, HER2 expression, and the number of positive lymph nodes were significantly higher in the patient group ($P < 0.0001$, $P < 0.0001$, and $P < 0.0001$, respectively). A statistically significant difference was also observed in the hormone receptor status (ER/PR) ($P = 0.043$), while there was no significant difference in the age at diagnosis ($P = 0.224$).

Prognostic Indicators

Table 2. Prognostic Indicators Result.

Prognostic Indicator	Patient Group (Mean ± SD)	Control Group (Mean ± SD)	P-value
Tumor Grade	**2.40 ± 0.60**	**1.60 ± 0.50**	**0.0**
Ki-67 Proliferation Index (%)	**31.20 ± 8.70**	**15.30 ± 6.40**	**0.0**
Clinical Stage	**2.90 ± 0.80**	**1.30 ± 0.50**	**0.0**

The prognostic indicators show highly statistically significant differences between the two groups ($P < 0.0001$ for all indicators). Tumor grade, Ki-67 proliferation index, and clinical stage were significantly higher in the patient group, indicating a more aggressive nature of the disease in this group.

Biochemical Indicators

Table 3. Biochemical Indicators Result.

Biochemical Indicator	Patient Group (Mean ± SD)	Control Group (Mean ± SD)	P-value
CA 15-3 (U/mL)	**34.07 ± 14.05**	**25.35 ± 8.97**	**0.0004**
CEA (ng/mL)	**5.85 ± 2.34**	**3.56 ± 2.03**	**0.0**
CRP (mg/L)	**12.35 ± 6.33**	**6.80 ± 2.37**	**0.0**
LDH (U/L)	**286.70 ± 66.44**	**219.41 ± 48.92**	**0.0**

The biochemical indicators show statistically significant differences between the patient and control groups ($P < 0.0001$ for all indicators). The levels of four biomarkers, including CA 15-3, CEA, CRP, and LDH in the patient group were significantly higher compared with those in the normal subjects which indicating their potential utility as sensitive markers for both diagnosed and relapse/progress breast cancer. The differences in the biochemical indicators were statistically significant between two groups. Levels of CA 15-3, CEA, CRP, and LDH were significantly different between the patient group and control group ($p < 0.0001$ for all markers except for CA 15-3, where $p = 0.0004$).

Conclusions: Our results indicated that these markers could be helpful in the diagnosis and monitoring of breast cancer.

4. Discussion

These results underline the clinical relevance of the indicators evaluated in breast cancer diagnostics and follow-up. The much larger tumor size, the positivity of Her2neu expression and lymphonode-metastasis in the patient group is concordant with scientific reports [18], indicating these predictors are dominant prognostic factors for aggressiveness of disease and course. In the clinical staging for determining treatment strategy, primary tumor dimension and nodal positivity are very crucial; larger sizes of tumors and more number of positive nodes leads to a higher stage assessment [19]. Once again, the data of tumor grade, Ki-67 proliferation index and clinical for survival group could give evidence that more malignant biological behavior existed among a majority of patients. Within the tumour, there is also an increase in staining of Ki-67, a marker for proliferation of cancer cells and often associated with a poorer prognosis [20]. This is consistent with prior reports showing robust correlations of these markers to clinical progression and responsiveness to therapy [21].

Regarding biochemical markers, the study found higher levels of CA 15-3, CEA, CRP and LDH in patients' serum than in healthy controls; these increases were statistically significant. CA 15-3 and CEA are tumor markers that can be used to monitor breast cancer, and if the levels of these markers in serum are high, it often indicates that the disease has developed or metastasized [22]. Consistent with our results, several previous studies have showed that increased levels of CA 15-3 or CEA were associated with a poor prognosis in breast cancer patients [23].

Markers of inflammation such as C-reactive protein (CRP) have been associated with cancer in epidemiological studies and elevated levels of CRP are found in patients with various types of cancers which is related to systemic inflammation that may support tumor formation and metastasis development [24]. A large body of evidence has consistently linked higher CRP levels with both increased risk for breast cancer [10] and poorer prognosis after diagnosis [11,12]; The increase in lactate dehydrogenase (LDH), an enzyme that is produced during tissue damage and hypoxic states could also indicate the higher rates of cancer cells metabolism and the worst prognosis in these patients [26].

The most important role of biomarkers tested in this study is to help understand the biology behind breast cancer by providing crucial prognostic and predictive outcome. Personalized Medicine in Breast Cancer One of the main pillars of tailored therapy to incident a more specific group of patients for targeted therapies and to profile each patient into different groups as low versus high disposed to relapse [27]. Similarly, the expression of HER2 and Ki-67 provides us with evidence to make a choice in regard to chemotherapy or targeted therapy which leads to improving patient outcomes [28]. Conclusions: This investigation indicating the significant role of diagnostic, prognostic and biochemical markers in KirkukI Male breast cancer diagnosis. Such markers can assist in better accuracy of diagnosis, determine an increased risk of disease progression and support in treatment planning for the best possible outcome.

5. Conclusion

This study concluded that westernized dietary risk factors contribute towards the rise of breast cancer in Kirkuk Governorate reduce or eliminate then the incidence rates among Kurdish women. Here, we review these markers and their importance as useful breast cancer biomarkers for diagnosis, monitoring and prognosis of the disease. The increase in tumor size, HER2 expression, positive lymph nodes number, tumor grade, Ki-67 proliferation index clinical stage CA 15-3 CEA CRP and LDH levels in the patient group are found to be consistent with the aggressive nature of disease and exhibits an example

of advanced stage carcinoma. The study suggests further research on these markers to provide better diagnostic and therapeutic interventions for breast cancer patients in the area.

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